

# Hydroxypropyl Methylcellulose

## Processing

### Executive Summary

Hydroxypropyl methylcellulose (HPMC) was petitioned as an ingredient of hard capsules used for encapsulating powdered herbs. This use is petitioned as an alternative to gelatin (animal based) capsules. HPMC has many other uses as an emulsifier, thickening agent, stabilizer, gellant, and suspending agent.

HPMC is a cellulose ether, derived from alkali treated cellulose that is reacted with methyl chloride and propylene oxide. The NOSB approved powdered cellulose, a less processed material usually derived from wood pulp fiber, for use as a filtering aid and anti-caking agent in October of 2001.

All reviewers found that HPMC is synthetic and nonagricultural, but were not in agreement about its use in organic production. Two reviewers felt that due to the use of synthetic hazardous materials to produce HPMC, it is not compatible with use in organic products, and that alternatives can be developed. Another reviewer recommended that HPMC should be allowed, and restricted for use only in non-gelatin hard capsules, finding a lack of alternatives for this use. Two reviewers supported use in products labeled “made with organic (specified ingredients),” while one believes it should be prohibited for all uses

### Summary of TAP Reviewer Analysis<sup>1</sup>

#### 95% organic

Synthetic / Non-Synthetic:	Allowed or Prohibited:	Suggested Annotation:
Synthetic (3) Non-synthetic (0)	Allowed (1) Prohibited (2)	In hard non-gelatin capsules

#### Made with organic (70% or more organic ingredients)

Synthetic / Non-Synthetic:	Allowed or Prohibited:	Suggested Annotation:
Synthetic	Allowed (2) Prohibited (1)	(Reviewer 2) In hard non-gelatin capsules (Reviewer 3) Only for hard capsule applications

### Identification

**Chemical Name(s):**

hydroxypropylmethyl cellulose, 2-hydroxypropyl ether of methyl cellulose

**Other Name(s):**

propylene glycol ether of methylcellulose, 2-hydroxypropyl methyl ether, modified cellulose, hypromellose, HPMC, MHPC, carbohydrate gum

**Trade Name(s):**

Benecel®MP643, Isopto-Tears; Methopt; Poly-Tears; Tears Naturale, Methocel E, Methocel F, Methocel K Methopt, Pharmacoat ®/Metolose

**CAS Number:** 9004-65-3**Other Codes:**

INS number: 464; E 464

<sup>1</sup> This Technical Advisory Panel (TAP) review is based on the information available as of the date of this review. This review addresses the requirements of the Organic Foods Production Act to the best of the investigator's ability, and has been reviewed by experts on the TAP. The substance is evaluated against the criteria found in section 2119(m) of the OFPA [7 USC 6517(m)]. The information and advice presented to the NOSB is based on the technical evaluation against that criteria, and does not incorporate commercial availability, socio-economic impact, or other factors that the NOSB and the USDA may want to consider in making decisions.

## Characterization

### Composition:



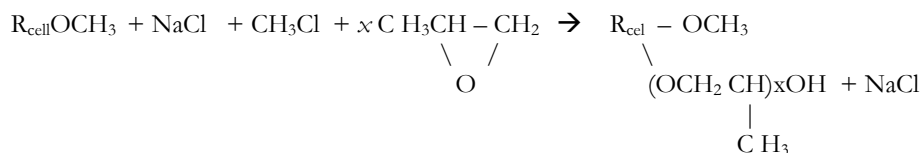
### Properties:

White to off-white fibrous powder or granules, swells in water to produce a viscous colloidal solution, non-ionic. Dissolves slowly in cold water, insoluble in hot water, soluble in most polar solvents, insoluble in anhydrous alcohol, ether, and chloroform. Aqueous solutions are surface active, form films upon drying and undergo reversible transformation from sol to gel upon heating and cooling (FCC 1996, Ash 1995, Budavari, 1996).

### How Made:

HPMC is considered to be part of the group of compounds known as cellulose ethers. See the TAP review for cellulose (NOP, 2001) for details of cellulose manufacturing, as well as the process for manufacture of microcrystalline cellulose (MCC). Many derivatives have been developed from cellulose, involving more drastic chemical modification of the basic cellulose molecule (Whistler, 1990). Various reaction products with methyl chloride are known as the methyl celluloses. This group includes carboxymethylcellulose (CMC) or cellulose gum; hydroxypropylmethylcellulose (HPMC) or carbohydrate gum; and methyl cellulose (MC, INS no. 461) or modified vegetable gum (Whistler, 1997). Methylcellulose is derived from alkali cellulose reacted with methyl chloride that adds methyl ether groups. The MC is then also reacted with propylene oxide to form HPMC. Other methyl cellulose derivatives include hydroxyethylmethylcellulose (HEMC), and hydroxybutylmethylcellulose (HBMC) (Whistler 1997, Kirk Othmer 1993).

The cellulose ethers are manufactured by a reaction of purified cellulose with alkylating reagents (methyl chloride) in presence of a base, typically sodium hydroxide and an inert diluent. The addition of the base in combination with water activates the cellulose matrix by disrupting the crystalline structure and increasing the access for the alkylating agent and promotes the etherification reaction. This activated matrix is called alkali cellulose (Kirk-Othmer, 1993). During the manufacture of HPMC alkali cellulose reacts with methyl chloride to produce methyl cellulose and sodium chloride. Side reactions of the methyl chloride and sodium hydroxide produce methanol and dimethyl ether by-products. The methylcellulose is then further reacted with the staged addition of an alkylene oxide, which in the case of HPMC is propylene oxide (Kirk Othmer, 1993; Dow, 2002).



After this reaction, MC and HPMC are purified in hot water, where they are insoluble. Drying and grinding completes the process.

Cellulose quality is measured by the content of alpha-cellulose, which is that portion insoluble in 18% alkali. Highly purified forms (over 99% alpha cellulose) are used to make the derivatives such as the cellulose gums, including sodium carboxymethylcellulose, methylcellulose and hydroxypropylmethylcellulose.

Methyl chloride (CH<sub>3</sub>Cl) is colorless gas with a faint, sweet odor that is not noticeable at dangerous concentrations. Synthetic forms are a chlorinated hydrocarbon derived from petroleum, and a suspected carcinogen. (Lewis, 1992; NJ 1998). It is also generated from incineration of municipal and industrial waste; though natural sources primarily oceans and biomass burning constitutes most of the global release into the environment. (WHO, 2001)

Propylene oxide is also a petroleum derivative, with a large volume and importance in the polyurethane and surfactant industry (Kirk-Othmer, 1996). There are two principal processes used: the traditional chlorohydrin process and indirect oxidation by the hydroperoxide process that uses a molybdenum catalyst. Both processes start with propylene (propene) derived from cracking of petroleum. The chlorohydrin process involves reaction of propylene (CH<sub>3</sub>CH=CH<sub>2</sub>) and chlorine in the presence of water to produce two isomers of propylene chlorohydrin. This is followed by dehydrochlorination using caustic soda or lime to produce propylene oxide and salt. The hydroperoxide process involves oxidation of propylene to PO by an organic hydroperoxide, producing an alcohol as a co-product. One of the possible alcohols (tert-butanol, TBE) produced as a by-product from this process is used as feedstock for MTBE, a gasoline additive (Kirk-Othmer 1996).

**Specific Uses:**

Food uses include as emulsifier, thickening agent, stabilizer, gellant, film former, protective colloid, fat barrier, suspending agent in food products; including bakery goods, ice cream, breadings, dressing, salad dressings, sauce mixes (FCC, 1996; Ash, 1995.) The gels produced from the cellulose derivatives have desirable fat like functional properties, including creaminess, fat like mouth-feel, stability, texture modification, increased viscosity and glossy appearance of high fat emulsions. (Brannen, 2002) HPMC is preferred for oil emulsions, including mineral oil, vitamin A, olive, soy and flavor oils (Greminger, 1973).

In baked products they improve tenderness and extend shelf life. A major use is in nondairy whipped toppings, also used in as emulsifiers in handcreams and lotions. They are resistant to bacterial decomposition. Methyl cellulose is sometimes called modified vegetable gum, HPMC is occasionally called carbohydrate gum (Whistler 1997).

HPMC has many pharmaceutical uses, as a drug carrier, a coating agent, a tableting agent, an emulsifier in ointments (Greminger, 1973). It is also used in ophthalmic solutions (Robert, 1988, USP 1995) and as a slow release agent. It is widely used in personal care products as a thickening agent and foam stabilizer (Dow, 2002).

The petitioned use is as an ingredient of hard capsules used for encapsulating powdered herbs. These are considered to be “vegetable” capsules, as they are an alternative to gelatin (Smithers, 2002).

**Action:**

Methyl celluloses (MC and HPMC) have properties known as reversible thermal gelation that is the basis for many applications- they form gels when heated but return to solubility when cooled. They are used to reduce the amount of fat in foods by 1) imparting fatlike properties, including richness and providing a slippery “mouthfeel” and 2) reducing the absorption of fat in products being fried (Whistler 1997).

**Combinations:**

Hundreds of US, EU and Japanese patents have been granted to various combinations of HPMC and other ingredients used as capsules. These include carageenan, potassium chloride, polyvinyl chloride, polyethylene glycol, ammonium ions, gelatin, catechin, mannan gums, locust bean gum, pectin, glycerin, acetic acid, calcium gluconate, sucrose fatty acid esters (Chiba 1990, Matsuura 1993, Tanida 1998, Yamamoto 2002, Yang 2002).

**Status**

**Historic Use:** Patents disclosing the process for making HPMC were granted to A. B. Savage of Dow Chemical in 1958 (Greminger, 1973).

**OFPA, USDA Final Rule:**

HPMC may be considered a synthetic ingredient as per 7 USC 6510(a) and allowed if on the National List as stated at 7 USC 6510(a)(4).

HPMC does not appear on the National List of allowed non-organic ingredients at 7 CFR 205.605 or as a non-organically produced agricultural products allowed as ingredients in or on processed products at 7CFR 205.606. The NOSB voted to approve powdered cellulose for use as a filter aid and anti-caking agent, and in regenerated casings (used for hot dogs and sausage) in October 2001. The NOSB did not approve the use of microcrystalline cellulose at that time. The NOSB also approved gelatin for use in organic food processing in May 2002, and decided that gelatin is an agricultural product that must be from organic sources when available, and therefore implicitly allowed under 7CFR 205.606.

**Regulatory: EPA/NIEHS/Other Sources**

EPA – included on List 4B, “Inerts which have sufficient data to substantiate they can be used safely in pesticide products.”

EPA – Clean Air Act Amendments – final rule for National emission standards for hazardous air pollution (NESHAP) includes cellulose ethers production source category as including major sources of emissions of hazardous air pollutants. (FR67:112: 40044) June 11, 2002.

NTP/NIEHS.: not listed in the National Toxicology Program database .  
OSHA- No hazard label required

FDA Status:

<b>21 CFR Listing</b>	
172.874	For direct food use (b) as an emulsifier, film former, protective colloid, stabilizer, suspending agent, or thickener, in accordance with good manufacturing practice
175.105	Indirect food additive as component of adhesives
175.300	Resinous and polymeric coatings
177.1960	Indirect Food Additives: Polymers --Substances for Use as Basic Components of Single and Repeated Use Food Contact Surfaces : as co-polymer with Vinyl chloride-hexene-1

Source EAFUS, 2001

**Status among U.S. Certifiers**

Not listed in any published standards. May have been allowed as ingredients for capsules by some US certifiers in “made with organic” or organic products prior to implementation of NOP rule.

*California Certified Organic Farmers (CCOF)* – CCOF Manual Two: USDA Requirements for Organic Producers (Dec. 2001) Not listed.

*Oregon Tilth Certified Organic (OTCO)* – Oregon Tilth Certified Organic Standards, Oct. 8, 2001. Not listed in Section 8, National List that accompanies the standards.

*Organic Crop Improvement Association International (OCIA)* OCIA Standards Manual NOP Standards plus OCIA International Requirements 2002: Not listed

Quality Assurance International (QAI) – Program Policies (web site July 2002) 5.2 Acceptable and Prohibited Materials - Until full implementation of the NOP, the general criteria used by QAI for determining the acceptability of materials is that specified by the Organic Materials Review Institute (OMRI). Clients will be notified of which materials they currently use that will not comply, upon full implementation of the NOP. All approvable materials must be on the National List for any product to be certified after October 21, 2002. [No specific reference to HPMC.]

*Texas Department of Agriculture (TDA) Organic Certification Program* – TDA Organic Certification Program Materials List (February 2000) Not listed

*Washington State Department of Agriculture (WSDA) Organic Food Program* – Chapter 16-158-060 WAC (rev. January 18, 2001), not listed.

**International**

CODEX – Not listed

EU 2092/91 – Not listed.

IFOAM – Not listed. (IFOAM IBS 2000)

Canada – (1999). Not listed in Appendix C, Permitted Substances for Processing. .

**Section 2119 OFPA U.S.C. 6518(m)(1-7) Criteria**

- The potential of the substance for detrimental chemical interactions with other materials used in organic farming systems.*  
This material is being considered for use in processing applications and does not directly interact with farming systems.
- The toxicity and mode of action of the substance and of its breakdown products or any contaminants, and their persistence and areas of concentration in the environment.*  
See processing criterion number 2.
- The probability of environmental contamination during manufacture, use, misuse, or disposal of the substance.*  
See processing criterion number 2.
- The effects of the substance on human health.*  
See processing criterion number 3.

5. *The effects of the substance on biological and chemical interactions in the agroecosystem, including the physiological effects of the substance on soil organisms (including the salt index and solubility of the soil), crops and livestock.*  
Not intended for use in soil systems.
6. *The alternatives to using the substance in terms of practices or other available materials.*  
See processing criteria numbers 1 and 7.
7. *Its compatibility with a system of sustainable agriculture.*  
See processing criterion number 6.

### **Criteria from the February 10, 1999 NOSB Meeting**

A PROCESSING AID OR ADJUVANT may be used if:

1. *It cannot be produced from a natural source and has no organic ingredients as substitutes.*

HPMC is derived from cellulose which itself was determined to be a synthetic by the NOSB. There is no known way to produce HPMC naturally, although there are natural alternatives for use as capsule ingredients and as thickeners and gelling agents. See discussion of alternatives under number 7.

2. *Its manufacture, use, and disposal do not have adverse effects on the environment and are done in a manner compatible with organic handling as described in section 6510 of the OFPA.*

Cellulose pulp manufactured from wood products historically has many environmental concerns. Recovery of waste chemicals, such as caustics, sulfites, and bleaching agents are important to avoid water pollution. The organic waste liquor substances may be disposed of by combustion, resulting in odors and air pollution (Kirk-Othmer, 1993b).

Cellulose ethers are not known themselves to have adverse environmental effects. (Kirk-Othmer 1993) However the EPA final rule to amend the Clean Air Act of 1990 for National Emission standards for hazardous air pollution (NESHAP) includes cellulose products manufacturing (which includes viscose cellulose and cellulose ethers) as a major sources of emissions of hazardous air pollutants. (HAP) This new rule (June 2002) will require all major sources to reduce HAP emissions to meet maximum achievable control technology (ACS, 2002).

Methyl chloride is considered hazardous and is regulated by OSHA, NIOSH, DOT, DEP and EPA. It is highly flammable. It has been subject of increased regulation for worker exposure (KSU 2002). It is released in the atmosphere during production, incineration of as well as burning biomass, and naturally from the ocean. It is considered an ozone depleting substance and estimated to contribute 15% of the total equivalent of effective stratospheric chlorine. It has less effect than other ozone depleting compounds (CFCs) and is not thought to be a significant contributor to global warming. The main degradation path in the environment is through volatilization, as it is slowly hydrolyzed in soil and groundwater, but little information is known about biodegradation (WHO 2001). Methyl chloride is readily absorbed in human lungs and causes neurotoxicity, lung irritation, dizziness, drowsiness, blurred or double vision, and may damage liver and kidneys. (NJ 1998, WHO 2001) Animal studies show carcinoma and mutagenic effects, and it is a suspected human carcinogen and weak mutagen (WHO, Lewis 1992).

Propylene oxide has a half-life of 3-10 days in the atmosphere. It reacts with hydroxide, producing formaldehyde and acetaldehyde. In water it is hydrolyzed to propylene glycol or can react with halides to form halohydrins. It can also be degraded to propylene glycol by microorganisms. Persistence as propylene oxide in the environment is unlikely due to high reactivity. (Kirk Othmer 1996)

3. *If the nutritional quality of the food is maintained and the material itself or its breakdown products do not have adverse effects on human health as defined by applicable Federal regulations.*

No adverse toxicological effects are reported for cellulose ethers in general. Hazards from direct use are related to the formation of flammable dusts when finely divided and suspended in the air, which can result in explosion if ignition source is supplied. Good housekeeping, appropriate design and operation of equipment can minimize this risk. (Kirk-Othmer 1993)

HPMC used in food use does not have an impact on the nutritional quality of the food, as the methylcelluloses are not digestible and make no caloric contribution to the diet (Whistler 1990).

4. *Its primary purpose is not as a preservative or used only to recreate/improve flavors, colors, textures, or nutritive value lost during processing except in the latter case as required by law.*

Cellulose and its derivatives have many uses that include manipulation of textures. They do not have an impact on flavor, color, or nutritive value. Microcrystalline cellulose and cellulose gums are used to substitute for fat in many reduced fat products, including low-fat sausages and hot dogs (Whistler 1997; Mittal 1993; Barbut 1996). HPMC is used to provide a barrier to oil absorption in deep fat fryers for doughnuts and improve crispy texture. It is used to improve the sheen and clarity of canned pie fillings (Greminger 1973).

HPMC used in capsules provides a means of delivering pharmaceuticals, supplements, and herbs or liquid extracts in a method that preserves activity and stability of the product (Matsuura 1993, Nagata 2001). Capsule and supplement manufacturers claim that the masking of strong taste and odor of extracted herbs and supplements is an advantage of capsule formulation (Capsugel 2002, Revival Farm 2002).

5. *Is Generally Recognized As Safe (GRAS) by FDA when used in accordance with Good Manufacturing Practices (GMP), and contains no residues of heavy metals or other contaminants in excess of FDA tolerances.*

FDA considers HPMC to be a permitted direct and indirect food additive for specific uses at 21CFR 172.874 (see Status.) This listing states: "The food additive hydroxypropyl methylcellulose may be safely used in food ...". Although it is not listed as GRAS (in 21 CFR 182), it is considered a permitted food additive. Methyl cellulose is listed as GRAS for multipurpose use at 21CFR 182.1480.

Food Chemical Codex standard of identity includes the following limits (1996):

- Assay for methoxyl groups: within the range claimed by the vendor for any product type between a minimum of 19% and a maximum of 30% of methoxyl groups (--OCH<sub>3</sub>).
- Heavy metals: (as Pb) not more than 10 mg/kg
- Loss on drying: not more than 5.0%
- Residue on ignition: not more than 1.5%... to 3.0% [for different viscosities]
- Viscosity: The viscosity of a solution containing 2 g in each 100g is not less than 80% and not more than 120% of that stated on the label for viscosity types of 100 centipoises or less, and not less than 75% and not more than 140% of that stated on the label for viscosity types higher than 100 centipoises.

FDA regulations at 21CFR 172.874 require that the additive complies with the definition and specifications prescribed in the National Formulary, 12th edition. The USP monograph-NF 18 (USP 1995) specifies degree of substitution for methoxy groups, viscosity, loss on drying, and residue on ignition.

6. *Its use is compatible with the principles of organic handling.*

A basic principle of organic handling is to minimize the use of additives. The use of a non-organic additive to replace fat or provide texture characteristics not present in the natural food is not compatible with criteria 1 and 4.

The use as an ingredient in capsule formulation may be desirable in order to provide a non-animal source of capsules to vegetarians, those that have religious restrictions regarding animal derived products, or those concerned about the use of gelatin and the possible link to bovine spongiform encephalopathy (BSE, or mad cow disease) (Honkanen, 2002, Thorne 2001).

7. *There is no other way to produce a similar product without its use and it is used in the minimum quantity required to achieve the process.*

Alternative gelling agents and thickeners include starch, carrageenan and plant gums (Veg. Soc. 2002) and appear on the National List.

For capsules, a number of other processes have been patented and commercialized. These include soft agar capsules (Fuji, 1990), polymers composed of gellan, carrageenan and mannan gums (Winston 1993), modified starches and carrageenan (Tanner, 2002., Vertese 2002, and Christen 1975). Some of these alternatives are described as "soft" or "gel" capsules and may have different storage or keeping properties than "hard" capsules that are made from HPMC. HPMC has advantages over traditional gelatin capsules in that it is not chemically as reactive and eliminates problems of reaction between drugs and capsule shell. HPMC capsules have naturally low moisture content (30-50% of the gelatin capsules) and are more suited for drugs that are water unstable (Ogura 1998, Honkanen 2002). Another alternative to encapsulated herbs is to provide herbs in powdered or tincture form.

#### **Additional questions asked of reviewers**

1. Are you aware of any other alternative capsule materials that would be suitable for organic use?
2. Do you think any alternative capsule materials could be produced organically?

3. Do you have any knowledge of commercial availability of alternative types of capsule described above? Are they suitable for similar purposes as HPMC?
4. If you were an inspector evaluating the percentage of organic ingredients in an encapsulated herb supplement, do you think it is possible for such a product to make an “organic” claim – 95% organic ingredients, or a “made with organic” claim – 70% organic ingredients?
5. Do you know if any certifiers were allowing HPMC? Have you seen or do you know about any currently certified organic products in capsule form?

## **TAP Reviewer Discussion**

### **Reviewer 1** [Ph.D, Food Science and nutrition professor with inspection and certification experience, Western U.S.]

#### *NOSB Processing Criteria Evaluation*

1. *It cannot be produced from a natural source and has no organic ingredients as substitutes.*

I agree with the criteria evaluation, with additional comments.

Hydroxypropyl methylcellulose is manufactured from purified cellulose determined to be synthetic by NOSB. It is prepared by a series of chemical modification reactions, utilizing hazardous materials such as methyl chloride. Further review of the literature indicates no alternative commercial manufacturing process that uses less toxic components or organic ingredients.

2. *Its manufacture, use, and disposal do not have adverse effects on the environment and are done in a manner compatible with organic handling as described in section 6513 of the OFPA.*

Manufacture of HPMC utilizes both methyl chloride and propylene oxide. Propylene oxide in an alkaline environment produces two known carcinogens- formaldehyde and acetaldehyde. Overall the manufacturing process is not consistent with sustainable and/or organic scientific principles.

3. *If the nutritional quality of the food is maintained and the material itself or its breakdown products do not have adverse effects on human health as defined by applicable Federal regulations.*

Additional computer literature searches did not reveal any peer reviewed scientific papers that indicated HPMC affected or impacted the nutritional quality of food products. Most applications to food systems use 0.1 to 0.5% HPMC for specific functional (physico-chemical) rather than nutritional reasons.

4. *Its primary purpose is not as a preservative or used only to recreate/improve flavors, colors, textures, or nutritive value lost during processing except in the latter case as required by law.*

I agree with the criteria evaluation

5. *Is Generally Recognized As Safe (GRAS) by FDA when used in accordance with Good Manufacturing Practices (GMP), and contains no residues of heavy metals or other contaminants in excess of FDA tolerances.*

I agree with the criteria evaluation

6. *Its use is compatible with the principles of organic handling.*

Clearly HPMC is a synthetic food additive. It is highly chemically modified to impart its outstanding functional food applications. However, since it is not only synthetic, but manufactured using potentially hazardous chemical modifying agents, it is very difficult to argue that it is compatible with organic handling criteria. I am especially concerned with the use of propylene oxide, as a final alkaline oxide reactant, in the last stage of its manufacture and its potential to form formaldehyde and acetaldehyde.

7. *There is no other way to produce a similar product without its use and it is used in the minimum quantity required to achieve the process.*

I agree with the criteria evaluation, with additional comments.

Many alternatives exist. If a suitable gel cap is an absolute necessity research or additional formulation work should be directed at using NOP approved substances such as gelatin, alginic acid, alginates, glycerin, pectin, and the following gums: xanthan, arabic, guar, locust bean, carob bean, and carrageenan. It is entirely possible and probable that an alternative could be developed for HPMC that would be consistent with the organic process principles of the NOP.

As an alternative, powders or tinctures would provide a further alternative.

***Reviewer 1 Conclusion*** – Summarize why this material should be allowed or prohibited for use in organic systems.

I would like to complement OMRI for conducting an excellent literature search. It was difficult to find any new scientific information regarding the status of HPMC.

It is very difficult to argue that use of HPMC is compatible and consistent with the basic fundamental principles of organic handling and processing criteria. Suitable alternatives exist which are significantly more compatible with organic handling criteria and standards, especially gelatin which was approved by the NOSB in May 2002.

Hydroxypropyl methylcellulose is clearly a synthetic food additive that is listed as a permitted food additive by the FDA. It is a highly chemically modified additive which utilizes hazardous materials during its manufacture. Additionally, one of the reactants, propylene oxide may form formaldehyde and acetaldehyde, two known carcinogens. One can reasonably argue that manufacture of HPMC is not consistent with sound environmental stewardship and principles of organic handling. Furthermore, suitable alternatives may exist from materials approved by the NOP sections 205.605 and 205.606.

***Recommendation Advised to the NOSB:***

*The substance is:* Synthetic

*In a product labeled 95% organic*

*The substance should be* Prohibited (do not add to National List)

*In a product labeled "made with organic (specified ingredients)"*

*The substances should be* Prohibited (do not add to National List)

***Reviewer 2 [Ph.D. Biochemistry with food industry experience. Eastern U.S.]***

The packet of literature accompanying the TAP Review is exceptionally complete.

***NOSB Processing Criteria Evaluation***

*1. It cannot be produced from a natural source and has no organic ingredients as substitutes.*

I agree with the criteria evaluation.

*2. Its manufacture, use, and disposal do not have adverse effects on the environment and are done in a manner compatible with organic handling as described in section 6513 of the OFPA.*

I agree with the criteria evaluation

*3. If the nutritional quality of the food is maintained and the material itself or its breakdown products do not have adverse effects on human health as defined by applicable Federal regulations.*

The criteria evaluation [was] corrected or amended as follows: The first paragraph (human health effects of methyl chloride) [was moved to] criterion 2 above. The second paragraph responds to the question.

*4. Its primary purpose is not as a preservative or used only to recreate/improve flavors, colors, textures, or nutritive value lost during processing except in the latter case as required by law.*

I agree with the criteria evaluation

*5. Is Generally Recognized As Safe (GRAS) by FDA when used in accordance with Good Manufacturing Practices (GMP), and contains no residues of heavy metals or other contaminants in excess of FDA tolerances.*

The criteria evaluation needs to be corrected or amended as follows: The mention of methylcellulose is confusing and the statement 'HPMC . . . is not listed as GRAS' is misleading. 21CFR172.874 states: "The food additive hydroxypropyl methylcellulose may be safely used in food . . ." HPMC is an approved food additive.

The inclusion of the FCC information is nice, but the food additive regulation specifically states [21CFR172.874(a)]: "The additive complies with the definition and specifications prescribed in the National Formulary, 12th edition."

The document should disclose NF requirements in response to this question.

*6. Its use is compatible with the principles of organic handling.*

I agree with the criteria evaluation., which needs to be corrected or amended as follows:

The first paragraph deals with general use as a gelling agent or thickener. The paragraph is correct but the petitioned use is for something else. The second paragraph addresses the question but needs to differentiate more clearly between "hard" and "soft" capsules.

7. *There is no other way to produce a similar product without its use and it is used in the minimum quantity required to achieve the process.*

The criteria evaluation needs to be corrected or amended as follows: See suggestion above.

Consideration should be given to listing here the primary reason why ingestible materials are put into capsules. Some herbs and some vitamins taste awful. Encapsulation enables consumption. This is alluded to under criterion 4 but it would be better (my opinion) to have it all in one place.

Note: [The TAP contractor] does not have the responsibility for providing ‘context’ for a petitioned use. However, in this case, it would be useful to TAP reviewers and NOSB members with no pharmaceutical industry experience to have more awareness of the types of “capsules.” I suggest the following ‘context’ under NOSB Criterion 7.

Capsules used for encapsulation of supplements and pharmaceuticals can be divided into two types, “soft” and “hard.” Soft capsules are commonly used for oily materials (e.g., Vitamin E, fish oil, vitamins suspended in oil). Hard capsules are commonly used for dry materials (e.g., granules, powders, etc.).

The “filling” of most soft capsules has a low moisture activity. The “filling” contains oil (think of lecithin or fish oil) or a non-aqueous fluid. Thus the reason that HPMC is not useful for soft capsules is probably NOT directly related to its hygroscopicity, but to its physical rigidity. Looking at soft capsules, the filling process is intimate to the creation of the capsule itself. One Japanese process actually forms the capsule around droplets of the “filling.”

Hard capsules are “hard” and are created so that they can be used on standard capsule filling machines by filling (“pouring”) a granular material into the capsule bottom and then closing the capsule by adding the top and then sometimes putting a seal around the juncture. Some materials need to be dry to be stable. Think of an herb. If wet, the vegetable matter can become moldy. When dry and appropriately sized, it will flow into a capsule bottom. The Wang patent extends this to a glycerol-based extract. Note that this patent indicates that a vegetable gelatin capsule can tolerate 100% humidity and 40 deg C (104 deg F) for 90 days.

The historical standard material used to make capsules is gelatin. Soft capsules can be made of materials other than gelatin, including only ‘non-synthetic’ materials. Examples of such ‘non-synthetic’ capsules may be those made with agar (Fuji Capsule Co., 1990), gellan/carrageenan/mannan gums (Winston et al. 1994), and a combination of agar-agar, bean protein and wheat (an OMX product). Agar is frequently referred to as “vegetable gelatin” (Cook’s Thesaurus). Supplement labels declaring “vegetable gelatin” may be referring to “agar” but this is not always certain.

In contrast to the natural options available for soft capsules, the only known non-gelatin hard capsules appear to be those made with cellulose ethers. HPMC seems to be the most suitable cellulose ether for hard capsule manufacture.

### **Responses to Additional Questions**

1. *Are you aware of any other alternative capsule materials that would be suitable for organic use?*

For soft capsules, those made with agar-agar or the combination of mannan, gellan and carrageenan could be “non-synthetic” and thus preferred for organic use. For hard capsules, no other non-gelatin (“vegetarian”) capsules are available other than those made with HPCM and similar methylcellulose derivatives. Note that excipients, colors, plasticizers and other additives used in capsules also need to be evaluated by the certifier/manufacturer to ensure organic compatibility.

2. *Do you think any alternative capsule materials could be produced organically?* The gellan and mannan sources for soft capsules might be producible organically. Other natural materials – agar-agar, carrageenan – are seaweed derivatives and would be wild-harvested.

3. *Do you have any knowledge of commercial availability of alternative types of capsule described above? Are they suitable for similar purposes as HPMC?* The internet has several examples of soft capsules that look acceptable for organic use but nothing for hard capsules except gelatin and cellulose ethers.

4. *If you were an inspector evaluating the percentage of organic ingredients in an encapsulated herb supplement, do you think it is possible for such a product to make an “organic” claim – 95% organic ingredients, or a “made with organic” claim – 70% organic ingredients?*

This is an excellent and complicated philosophical question. The net weight declaration of a supplement represents the weight of the active ingredient. Any excipients and inactive ingredients are rarely considered in the weight. The package weight (i.e., the capsule) is almost universally ignored. Hard capsules weigh very little so it may be that this package weight is insignificant compared to that of the active ingredient. This may not hold true

for soft capsules which are thicker and contain plasticizer (preferably glycerol). A soft capsule containing saw palmetto extract, for example, has lecithin as a diluent. Even tablets contain tableting aids (starch, dextrose, stearates). The NOSB should debate this question, “how is percentage organic calculated for a dietary supplement?”

5. *Do you know if any certifiers were allowing HPMC? Have you seen or do you know about any currently certified organic products in capsule form?*

I have no direct knowledge here. However, the internet site for Taylor's Organic Gardens indicates that this company has been a long-time leader in providing the finest herbs and spices and continues to have the largest selection of Certified Organic Herbs and Spices. They have established more sources for high-quality organic products throughout the world. All of their organic herbs and spices are certified by Quality Assurance International. These herbs and spices are sold in capsules and apparently are labeled as organic. They use “vegetarian capsules” made “from pure vegetable sources.” See [www.dnavitamins.co.uk/productpages/certifiedorganic.htm](http://www.dnavitamins.co.uk/productpages/certifiedorganic.htm).

Additional comment: The “vegetarian capsules” made with HPMC are frequently claimed to be “all natural” and made from “pure vegetable sources.” FDA, FTC and USDA have rules for the term “all natural” which would not cover HPMC. It would seem important for NOP not to appear to be endorsing an “all natural” claim for hard capsules made with HPMC. HPMC is synthetic and not “natural.”

**Reviewer 2 Conclusion** – *Summarize why this material should be allowed or prohibited for use in organic systems.*

Despite HPMC being a synthetic material, there appears to be no alternative means for making a ‘vegetarian’ hard capsule. Thus, I believe that it should be allowed in the ingestible packaging of organic ingredients that cannot use soft capsules. An unaddressed concern is that many capsules are colored; the source of color frequently is artificial/synthetic and thus not compatible with organic.

**Recommendation Advised to the NOSB:**

*The substance is:*            Synthetic , and Non-Agricultural

In a product labeled 95% organic

*The substance should be*    Allowed only with restrictions (annotation)

*Suggested annotation:*    in hard non-gelatin capsules

In a product labeled “made with organic (specified ingredients)”

*The substances should*    Allowed only with additional restrictions (annotation)

*Suggested annotation:* in hard non-gelatin capsules

**Reviewer 3** [PhD. Food Science, organic and natural foods industry consultant, Western U.S.]

**NOSB Processing Criteria Evaluation**

1. *It cannot be produced from a natural source and has no organic ingredients as substitutes.*

I agree with the criteria evaluation.

2. *Its manufacture, use, and disposal do not have adverse effects on the environment and are done in a manner compatible with organic handling as described in section 6513 of the OFPA.*

I agree with the criteria evaluation.

3. *If the nutritional quality of the food is maintained and the material itself or its breakdown products do not have adverse effects on human health as defined by applicable Federal regulations.*

I agree with the criteria evaluation.

4. *Its primary purpose is not as a preservative or used only to recreate/improve flavors, colors, textures, or nutritive value lost during processing except in the latter case as required by law.*

Many celluloses are used to modify textures. HPMC is not used specifically for that purpose. The use of capsules for delivery of powdered herbs is desirable as it masks unpleasant tastes and odors and allows a convenient “dosing” system for herbs.

5. *Is Generally Recognized As Safe (GRAS) by FDA when used in accordance with Good Manufacturing Practices (GMP), and contains no residues of heavy metals or other contaminants in excess of FDA tolerances.*

HPMC is a permitted food additive, but it is not GRAS for use in foods.

6. *Its use is compatible with the principles of organic handling.*

The use of a highly chemically modified material is not compatible with the principles of organic handling. There are many toxic chemicals used in the manufacture of these capsules and consequently there is toxic waste produced. While it is laudable to provide alternatives to gelatin for vegetarians, it is concerning that these capsules are synthetic and are not compatible with organics.

7. *There is no other way to produce a similar product without its use and it is used in the minimum quantity required to achieve the process.*

At the present time, there is no alternative to producing “hard” gelatin capsules that are compatible with organics and it would take much research to develop a hard capsule that would comply.

Other alternatives for herb delivery include providing powdered herbs without the capsule, delivering organic tinctures and using a soft gel capsule with a liquid herb extract that would be more compatible with organic systems. (It may even be possible to develop an “organic” softgel, according to a recent patent.)

### **Response to Additional Questions**

1. *Are you aware of any other alternative capsule materials that would be suitable for organic use?*

For hard capsules, there do not appear to be any other options that would be compatible with organic systems. Softgels could not be specifically used for the application that the Petitioner requested, but could be used for herbal extracts as compared to powdered herbs in products.

2. *Do you think any alternative capsule materials could be produced organically?*

There are soft capsules available that are non-synthetic and therefore, would be more compatible with organic systems. In reading one of the patents referred to below regarding vegetable capsules (Winston, et al, 1994), it would appear that one or two of the formulas in the patent could actually be produced so as to be an organic softgel capsule.

3. *Do you have any knowledge of commercial availability of alternative types of capsule described above? Are they suitable for similar purposes as HPMC?*

There is no commercial availability that is available at the present time for softgels that would be organic in origin. There are no other sources of hard capsules other than the HPMC.

4. *If you were an inspector evaluating the percentage of organic ingredients in an encapsulated herb supplement, do you think it is possible for such a product to make an “organic” claim – 95% organic ingredients, or a “made with organic” claim – 70% organic ingredients?*

The answer to this question depends on the formulation of ingredients for a dietary supplement. Typically, they consist of powdered herbs with a significant amount of carrier/diluent such as maltodextrin, which is organic-compatible, but not available organic. There are other “carriers” such as cornstarch or rice flour that are available as organic. Without knowing the percentage of the total weight that is capsule material, it is hard to speculate, but it seems that a few products could reach an “organic” claim, but may qualify for “made with organic.”

5. *Do you know if any certifiers were allowing HPMC? Have you seen or do you know about any currently certified organic products in capsule form?*

I am not aware of any certifiers allowing the certified organic products in capsule form, although it seems that several manufacturers have “organic” lines that are being sold today. I am not sure on what basis they are currently making that determination.

### ***Reviewer 3 Conclusion – Summarize why this material should be allowed or prohibited for use in organic systems.***

This material does not appear to be consistent with the principles of organic handling. Its production uses hazardous and toxic chemicals and it is highly chemically modified. Its use is limited to powdered herbs, which may be delivered without the capsule or delivered in other formats such as liquid tinctures or softgels. If the herbs and carriers were compatible with organic systems, it could be used with a “Made With Organic” claim as the capsule is not compatible. This would hopefully, spur the development of more compatible systems to deliver an Organic claim.

Development of organic-compatible softgel systems would allow herbs to be delivered in dosed products.

### **Reviewer 3 Recommendation Advised to the NOSB:**

The substance is: Synthetic and Non-Agricultural

in a product labeled 95% organic

The substance should be Prohibited (do not add to National List)

in a product labeled “made with organic (specified ingredients)”

The substances should be Allowed only with additional restrictions (annotation)

Suggested annotation: Only for hard capsule applications

### **TAP Conclusion**

HPMC is a synthetic material that was requested for use in capsules for organic herb or supplement products. Alternatives to gelatin are desirable for vegetarians, and are available for use in soft capsules. Soft capsules are not suitable for all forms of supplements or herbal powders. Two reviewers do not consider HPMC to be compatible with organic principles and expressed concerns about the manufacturing process for HPMC. This concern was not shared by one reviewer, who found that the lack of alternatives was a compelling reason to allow for use only in non-gelatin hard capsules. Although alternatives for use in hard capsules are not available, herbal products can also be marketed as tinctures or powders. Two reviewers supported use in made with organic products; with an annotation of “for hard non-gelatin capsule applications” while one believes it should be prohibited for all uses.

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This TAP review was completed pursuant to United States Department of Agriculture Purchase Order 40-6395-0-2900.